

REMARKS

Entry of the foregoing and favorable reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. Section 1.112, and in light of the remarks which follow, are respectfully requested.

By the present amendment, claims 1 and 12 have been amended to recite “that catalyzes” and “that regulates” in lieu of “catalyzing” and “regulating.” New Claims 35 and 36 have been added. Support for this new claim appears at least on page 7 of the specification. Applicants submit that no new matter has been added via this amendment.

Claims 1 and 12 have been objected to for the recitation of “catalyzing” and “regulating.” As stated above, these claims have been amended, which should render this objection now moot.

Claims 12 and 13, 17 to 18, 20, 21, 30 and 32 to 34 dependent thereon, have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. For the following reasons, this rejection is respectfully traversed.

In rendering this rejection, the Examiner purports that it is not clear from claim 12 if the promoter is limited to a promoter of a methyl transferase gene or may be any plant expressible promoter.

Claim 12 recites that the promoter is **a plant expressible promoter** that regulates the expression of a nucleic acid coding for a methyl transferase. Also at least page 11 of the specification discloses that “any promoter permitting constitutive, spatial or temporal expression of a nucleic acid in a plant cell may be used for the implementation of the invention.” Thus it

should be clear from the claim as well as the disclosure in the specification that the promoter is a plant expressible promoter, which Applicants submit is clearly defined.

Therefore, in view of the above, withdrawal of this rejection is respectfully requested.

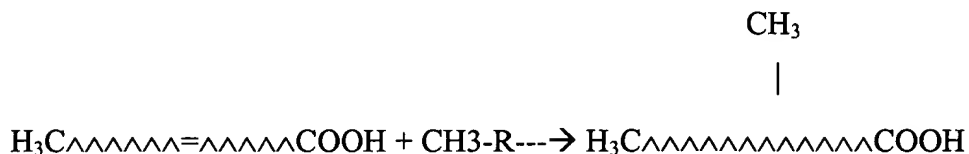
Claims 1, 2, 12, 13, 17 to 21, 23, 30 and 31 to 34 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to convey to one skilled in the art, at the time the application was filed, that the inventors had possession of the claimed invention. This rejection is respectfully traversed.

In rendering this rejection, the Examiner purports that the description of two methyl transferases set forth in the specification does not adequately define the entire genus that is claimed. Applicants respectfully disagree with the Examiner for the following reasons.

First of all it was well known in the art prior to the filing of the present invention that a methyl transferase is an enzyme that catalyzes the transfer of a methyl group from a methyl group donor. This enzyme has no other function except by acting to transfer a methyl group. Methyl transferases are also classified together in the standard enzyme classification system as falling under E.C. 2.1.1. Although there are several types of methyl transferases such as N-methyltransferases, S-methyltransferases and O-methyltransferases, these enzymes still function in the same manner; i.e., by transferring a methyl group to the respective places on the acceptor molecule whether it be at the N-position, the C-position or the S-position etc.

Likewise, it was also well known at the time of filing of the present application that plant cells contain various fatty acids, which are necessary for lipid metabolism in the plant. There are both saturated and unsaturated fatty acids in plant cells.

When a methyl transferase is present in the presence of an unsaturated fatty acid a methyl group is added to the double bond in the fatty acid such as set forth below:



Thus, due to the presence of a double bond in the unsaturated fatty acid, which is a source of electrons, an addition reaction is formed which permits the methyl group to always attach at the double bond, converting it to a single bond.

The Examiner asserts that the two described methyl groups in the specification do not entitle the Applicant to claim the entire genus. But, as demonstrated above, a skilled artisan would realize that since the enzyme methyl transferase only catalyzes the transfer of a methyl group and since the methyl group is only attached on the aliphatic chain of the fatty acid at a particular place, that the description of two methyl transferases in the specification is sufficient support for the inventors to have possession of the entire genus at the time of filing of the present application.

Therefore, in view of the above, withdrawal of this rejection is respectfully requested.

Claims 1, 2, 12, 13, 17 to 21, 30 and 31 have been rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. For the following reasons, this rejection is respectfully traversed.

In rendering this rejection, basically the Examiner purports that the specification is only enabled for those constructs which are set forth in the samples; i.e., tobacco plants and cyclopropane fatty acid synthase, deeming that the specification does not provide reasonable enablement for “the production of branched fatty acids in any plant with any gene that encodes

an enzyme that will transfer one or more alkyl groups to the double bond of an unsaturated fatty acid.” However the claims do not recite “an enzyme”, but rather a specific enzyme of methyl transferase.

As stated above in the lack of written description rejection, all methyl transferases function in the same manner; i.e., by transferring a methyl group to the respective places on the acceptor molecule. The exemplified cyclopropane fatty acid synthase is also an enzyme that transfers a methyl group to respective places on the acceptor molecule. Therefore, it functions in a similar manner as the methyl transferases. Hence, the person skilled in the art can easily produce the present invention without undue experimentation.

Furthermore, genes that encode methyl transferases were known in the art at the time of filing of the present application as evidenced by Annex I and II. Thus, the Examiner's concern that the genes encoding methyl transferases were “not in hand” should no longer be considered. Indeed, as the Federal Circuit stated in *S3 Inc. v. nVIDIA Corp.*, 259 F.3d 1364, 1371, 59 USPQ2d 1745 (Fed. Cir. 2001):

The law is clear that patent documents need not include subject matter that is known in the field of the invention and is in the prior art, for patents are written for persons experienced in the field of the invention.

Therefore, extensive elaboration of methyl transferase genes in the specification is simply not necessary, according to legal standards.

Furthermore, the Examiner deems that the teachings in the specification concerning methyl transferases are merely prophetic and thus unpredictable. There should be no legal weight given to this reasoning since as stated in *Gould v. Quigg*, 822F.2d 1074, 3 USPQ2d 1302 (Fed. Cir. 1987):

A disclosure is **not non-enabling because it sets forth prophetic examples**; it must be shown that the prophetic examples together with other parts of the specification are not enabling (emphasis added).

The Examiner has not attempted to explain why the other parts of the specification are not enabling, but simply relies on several references, which for at least the reasons presented in the Reply filed December 15, 2003, Applicants deem are irrelevant.

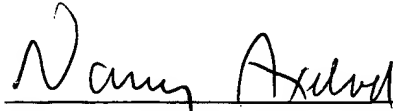
Moreover, the Examiner further purports that the presently claimed invention should be limited to that which was exemplified; i.e., tobacco plants, since “each plant species differs in biochemical composition with regard to the availability of precursor fatty acids.” However, the Examiner has not provided any scientific evidence to support this allegation.

The references of record previously cited in this rejection; i.e., Broun et al and DeLuca have nothing to do with the biochemical composition of precursor fatty acid in plants and do not even mention the enzyme methyl transferase, which is the subject enzyme of the presently claimed invention. Thus, the references are irrelevant to prove nonenablement since a person skilled in the art would realize that each enzyme is structurally and functionally different and therefore the Examiner’s reliance on Broun et al is misplaced. Secondly DeLuca at column 1, page 228N discloses the success of producing plants having an enzyme involved in fatty acid synthesis which redirected the pathway to medium chains instead of long chains. Thus the topic of DeLuca most closely related to the present invention of genetically engineered plants having to do with fatty acid synthesis was in fact not unpredictable as the Examiner purports.

Thus, in view of the above, withdrawal of this rejection is respectfully requested.

From the foregoing, favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

Respectfully submitted,

A handwritten signature in cursive script, reading "Nancy Axelrod", is written over a horizontal line.

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Date: September 27, 2004

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BLASTX+BEAUTY Search Results

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Content-type: text/html

Annex I

BLASTX+BEAUTY Search Results

BLAST search performed using the BLAST2 Search Service at EMBL.

BEAUTY post-processing provided by the Human Genome Center, Baylor College of Medicine.

BEAUTY Reference: Kim C. Worley, Brent A. Wiesc, and Randall F. Smith (1995). BEAUTY: an enhanced BLAST-based search tool that integrates multiple biological information resources into sequence similarity search results. Genome Research 5: 173-184.

RepeatMasker repeats found in sequence:
No Repeats Found.

BLASTX 2.0a8MP-WashU [25-Feb-1997] [Build 20:41:27 Feb 25 1997]

Reference: Gish, Warren (1994-1997). unpublished.
Gish, Warren and David J. States (1993). Identification of protein coding regions by database similarity search. Nat. Genet. 3:266-72.

Notice: statistical significance is estimated under the assumption that the equivalent of one entire reading frame in the query sequence codes for protein and that significant alignments will involve only coding reading frames.

Query= query_sequence
(639 letters)

Translating both strands of query sequence in all 6 reading frames

Database: nrdb Release 11.Mar.1998

300,102 sequences; 89,942,939 total letters.

Searching....10....20....30....40....50....60....70....80....90....100% done

Sequences producing High-scoring Segment Pairs:	Reading Frame	High Score	Smallest Sum	
			Probability P(N)	N
swiss P13444 METL RAT S-ADENOSYLMETHIONINE SYNTHETAS...	-1	631	1.4e-63	2
pironly A47151 A47151 methionine adenosyltransferase...	-1	628	3.0e-63	2
swiss Q00266 METL HUMAN S-ADENOSYLMETHIONINE SYNTHET...	-1	627	3.8e-63	2
swiss P31153 METK HUMAN S-ADENOSYLMETHIONINE SYNTHET...	-1	624	7.8e-63	2
swissnew P18298 METK RAT S-ADENOSYLMETHIONINE SYNTHET...	-1	623	1.3e-62	2
tramb D49357 HSSAMS1 1 product: "S-adenosylmethioni...	-1	615	6.9e-62	2
sptrembl O17680 O17680 S-ADENOSYLMETHIONINE SYNTHETA...	-1	630	6.2e-61	1
sptrembl Q95032 Q95032 S-ADENOSYLMETHIONINE SYNTHETA...	-1	624	2.7e-60	1
swiss P43281 METL LYCES S-ADENOSYLMETHIONINE SYNTHET...	-1	623	3.4e-60	1
sptrembl O22338 O22338 S-ADENOSYLMETHIONINE SYNTHETA...	-1	623	3.4e-60	1
swiss P49611 METK BRAJU S-ADENOSYLMETHIONINE SYNTHET...	-1	621	5.6e-60	1
swiss P50302 METL ACTCH S-ADENOSYLMETHIONINE SYNTHET...	-1	621	5.6e-60	1
swissnew Q96553 METM CATRO S-ADENOSYLMETHIONINE SYNT...	-1	618	1.2e-59	1
swiss P43280 METK LYCES S-ADENOSYLMETHIONINE SYNTHET...	-1	618	1.2e-59	1
swissnew P17562 METL ARATH S-ADENOSYLMETHIONINE SYNT...	-1	617	1.5e-59	1
swissnew P93254 METK MESCR S-ADENOSYLMETHIONINE SYNT...	-1	616	1.9e-59	1
swissnew Q96552 METL CATRO S-ADENOSYLMETHIONINE SYNT...	-1	615	2.4e-59	1
swiss P43282 METM LYCES S-ADENOSYLMETHIONINE SYNTHET...	-1	615	2.4e-59	1
swissnew P23686 METK ARATH S-ADENOSYLMETHIONINE SYNT...	-1	614	3.1e-59	1
swissnew P46611 METK ORYSA S-ADENOSYLMETHIONINE SYNT...	-1	613	4.0e-59	1
swiss P50305 METK CAEEL PROBABLE S-ADENOSYLMETHIONIN...	-1	613	4.0e-59	1
swiss P48498 METK PETHY S-ADENOSYLMETHIONINE SYNTHET...	-1	613	4.0e-59	1

BLASTX+BEAUTY Search Results

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swiss|P50306|METL CAEL PROBABLE S-ADENOSYLMETHIONIN... -1 613 4.0e-59 1
swissnew|P24260|METL DIACA S-ADENOSYLMETHIONINE SYNT... -1 612 5.0e-59 1
swiss|P47916|METK POPDE S-ADENOSYLMETHIONINE SYNTHET... -1 612 5.0e-59 1
swissnew|P93438|METL ORYSA S-ADENOSYLMETHIONINE SYNT... -1 611 6.4e-59 1
sptrembl|Q27522|Q27522 S-ADENOSYLMETHIONINE SYNTHETA... -1 611 6.4e-59 1
swiss|P40320|METK DROME S-ADENOSYLMETHIONINE SYNTHET... -1 584 1.0e-58 2
swiss|P50301|METK ACTCH S-ADENOSYLMETHIONINE SYNTHET... -1 609 1.0e-58 1
swiss|P50303|METM ACTCH S-ADENOSYLMETHIONINE SYNTHET... -1 608 1.3e-58 1
swissnew|Q96551|METK CATRO S-ADENOSYLMETHIONINE SYNT... -1 607 1.7e-58 1
swiss|P50299|METK HORVU S-ADENOSYLMETHIONINE SYNTHET... -1 607 1.7e-58 1
swiss|P49613|METL PEA S-ADENOSYLMETHIONINE SYNTHETAS... -1 605 2.8e-58 1
pironly|S66352|S66352 methionine adenosyltransferase... -1 605 2.8e-58 1
swiss|P50304|METK ASCIM S-ADENOSYLMETHIONINE SYNTHET... -1 584 3.4e-58 2
swiss|P49612|METK PEA S-ADENOSYLMETHIONINE SYNTHETAS... -1 601 7.4e-58 1
swiss|P50300|METK PINBN S-ADENOSYLMETHIONINE SYNTHET... -1 601 7.4e-58 1
sptremblnew|G2665652|G2665652 S-ADENOSYLMETHIONINE S... -1 572 3.0e-57 2
swiss|P48466|METK NEUCR S-ADENOSYLMETHIONINE SYNTHET... -1 563 5.4e-56 2
sptrembl|Q12642|Q12642 S-ADENOSYLMETHIONINE SYNTHETA... -1 563 5.4e-56 2
swiss|P10659|METK YEAST S-ADENOSYLMETHIONINE SYNTHET... -1 556 8.8e-56 2
trembl|J03477|SCSAM1 1 gene: "SAM1"; product: "S-ade... -1 552 2.3e-55 2
swiss|P19358|METL YEAST S-ADENOSYLMETHIONINE SYNTHET... -1 543 2.1e-54 2
trembl|U33057|SC9717 8 gene: "SAM2"; product: "Sam2p... -1 543 2.1e-54 2
pironly|S51671|S51671 methionine adenosyltransferase... -1 332 3.8e-51 2
sptrembl|Q34566|Q34566 S-ADENOSYLMETHIONINE SYNTHETA... -1 512 9.9e-51 2
swiss|P54419|METK RACSU S-ADENOSYLMETHIONINE SYNTHET... -1 502 1.1e-49 2
swissnew|P50307|METK STAAU S-ADENOSYLMETHIONINE SYNT... -1 485 9.9e-49 2
trembl|L36680|PSDENSINA 1 product: "S-adenosylmethio... -1 506 8.6e-48 1
sptremblnew|G2688287|G2688287 S-ADENOSYLMETHIONINE S... -1 470 5.6e-44 1

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Locally-aligned regions (HSPs) with respect to query sequence:

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Locus ID                               Frame -1 Hits
gi|127048                               |
gi|476917                               |
gi|417297                               |
gi|400245                               |
gi|127043                               |
gi|417297                               |
sptrembl|O17680|O1768                  |
sptrembl|Q95032|Q9503                  |
gi|1170938                             |
sptrembl|Q22338|Q2233                  |
gi|1346520                             |
gi|1709004                             |
swissnew|Q96553|METM                    |
gi|1170936                             |
gi|127045                               |
swissnew|P93254|METK                    |
swissnew|Q96552|METL                    |
gi|1170939                             |
gi|127041                               |
gi|1170937                             |
gi|1708998                             |
gi|1346523                             |
gi|1709005                             |
gi|127046                               |
gi|1346524                             |
swissnew|P93438|METL                    |
sptrembl|Q27522|Q2752                  |
gi|730019                               |
gi|1708995                             |
gi|1709006                             |

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Plant Gene Register PGR97-052

Annex II

Carlos Nicolas and Emilio Cervantes (1997) Cloning and Nucleotide Sequence of CaSAMs (Accession No. X85252), a cDNA Encoding SAM Synthetase from Germinated Chickpea Seeds (PGR97-052). *Plant Physiol.* 113: 1463

Cloning and Nucleotide Sequence of CaSAMs (Accession No. X85252), a cDNA Encoding SAM Synthetase from Germinated Chickpea Seeds.

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SAM synthetase (S-Adenosyl-L-Methionine Synthetase; ATP:L-Methionine S-Adenosyl Transferase; EC 2.5.1.6) is the enzyme catalyzing the synthesis of SAM from methionine and ATP. SAM (AdoMet) participates in an array of biochemical reactions as in the synthesis of threonine and methionine or the synthesis of the polyamines spermine and spermidine. As the universal methyl donor, SAM is involved in methylation of nucleic acids, proteins, fatty acids and polysaccharides. In plant metabolism, SAM is the precursor in ethylene biosynthesis and it acts also as a methyl donor for secondary metabolites like caffeic acid required for lignin biosynthesis, chalcones, isoflavones and putrescine derived alkaloids.

⇒ Many cDNAs encoding SAM Synthetases have been isolated up to date from bacteria, yeast, animals and plants (see Wittaker *et al.*, 1995). In plants, increases in SAM synthetase gene transcripts have been described in tissues undergoing lignification, such as stems and roots in *Arabidopsis* (Peleman *et al.*, 1989) or after treatment of alfalfa plants with elicitors, simultaneously with the induction of mRNAs encoding enzymes of lignin biosynthesis (Gowri *et al.*, 1991). Induction of SAMs mRNA has been also described during corolla elongation in petunia (Izhaki *et al.*, 1996).

CaSAMs cDNA was cloned during the differential screening of a cDNA library made from RNA of germinated chickpea cotyledons previously reported (Cervantes *et al.*, 1996). In this experiment it was isolated as a cDNA to a putative ethylene up-regulated, norbornadiene repressed, mRNA. Further experiments to demonstrate the involvement of ethylene in its regulation have not been conclusive.

During seed development and dessication SAMs mRNA was detected as a constitutive transcript in northern blots, but it notably increased in seeds during the first hours after imbibition and after radicle emergence. More details of the regulation will be reported elsewhere.

Table 1. Characteristics of CaSAMs from chickpea (*Cicer arietinum*, L.).

Organism:
Cicer arietinum, L.

Source:

cDNA library in Lambda-ZAP constructed from poly(A)+ extracted from cotyledons of germinating seeds (48 hours after imbibition).

Clone type; Designation:
cDNA; CaSAMs.

Method of isolation:

Differential screening. Replicas of the library were hybridized to labelled cDNA prepared from cotyledons of either seeds imbibed in water or seeds imbibed in 2ml L-1 norbornadiene for 48 hours. SAMs was isolated as a clone specifically labelled in the control (without norbornadiene)treatment.

Sequencing strategy:

Manually, both strands, using T7 polymerase (Pharmacia) and double stranded templates.

Method of identification:

Sequence comparison with GenBank/EMBL data bases.

Features of the cDNA:

cDNA is 1411 bp in length, including a complete ORF and a putative polyadenylation signal at position 1288.

Features of the predicted amino acid sequence:

The ORF consists of 394 amino acids. The mature protein has a predicted molecular weight of 43372

Expression characteristics:

CaSAMs transcript is detected through all development of seeds at a low, constitutive level increaseing notably in the first hours after imbibition.

Literature Cited

Cervantes E, Nicolas C, Gonzalez B, Iturriaga EA (1996) Isolation and expression characteristics of CaPR-10a, an IPR coding cDNA from chickpea seeds. (PGR95-115). *Plant Physiol* 110: 335

Gowry G, Bugos RC, Campbell WH, Maxwell CA, Dixon RA (1991) Stress responses in alfalfa (*Medicago sativa* L.) X. Molecular cloning and expression of S-Adenosyl-L-Methionine:Caffeic Acid



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